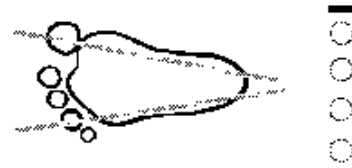


NEWBORN SCREENING



August 2001

Be Kind To Tiny Feet

A newsletter of the Newborn Screening Program and the Newborn Screening Laboratory

HEMOGLOBINOPATHIES Second Edition

Follow-up procedures for hemoglobinopathy screening and basic education

Hemoglobinopathy Screening Delayed

The Utah Department of Health worked hard to add hemoglobinopathies to the newborn screening panel around the beginning of July 2001. However, delays were incurred while changing the Rule (R398-1) to add hemoglobinopathies and in developing the computer software for the follow-up piece. The Isoelectric Focusing lab is set-up and ready to start screening blood spot samples.

EDITOR'S CORNER

The Utah Department of Health has designed the hemoglobinopathy screening and follow-up protocols with a strong emphasis on *education*. We realize that there are many hemoglobinopathies (over 600 variants have been identified) and the follow-up process could be complicated. All of our letters, mailed to healthcare providers and families, for the follow-up of unusual hemoglobin patterns, will include education about the hemoglobin pattern. There is a full time nurse available, Jan Bagley, RN, (Editor) Monday through Friday from 8 AM to 5 PM, at 801-584-8260, to answer any questions you may have as we start screening for hemoglobinopathies.

Watch for the *Third Edition* on Hemoglobinopathies!
This last edition will cover the Genetics piece of hemoglobinopathies.



Division of Community & Family Health Services, Newborn Screening Program: (801) 584-8256 fax: (801) 536-0966
Division of Epidemiology & Laboratory Services, Newborn Screening Laboratory: (801) 584-8400 fax: (801) 584-8486

SICKLE CELL TRAINING

Shirley Bleak, FNP-C, from the Department of Hematology, at Primary Children's Medical Center and Jan Bagley, RN, (ME!) from the Utah Department of Health, Newborn Screening Program, attended Sickie Cell Training on June 5th to June 7th. The California Department of Health Services, Genetics Disease Branch, Newborn Screening Section offered the program. It was held at the new Valley Children's Hospital in Madera, California. (Shirley and I were both very impressed with the new hospital. It looks a lot like Disneyland!).

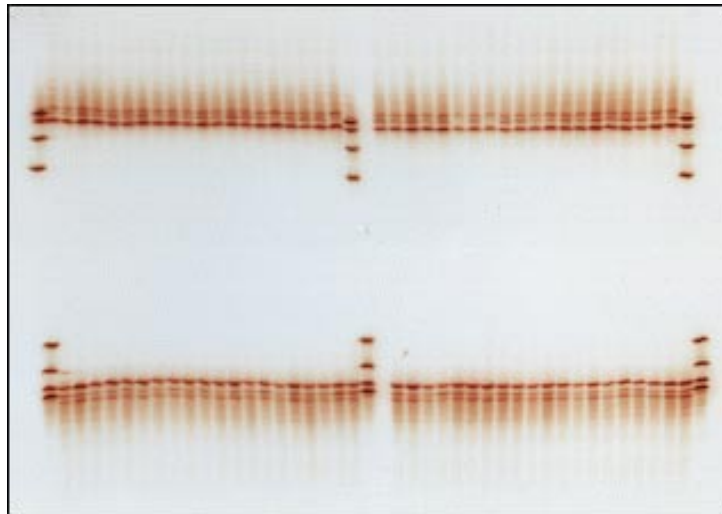
We learned the basics from our experienced friends in California about screening for hemoglobinopathies. The first sickle cell counselor-training program in California was started in Los Angeles in 1972. In 1980, the training expanded to serve the needs for the entire state. In 1990, when screening for hemoglobinopathies was added to the statewide newborn screening program, the training program was revised to meet the needs for hemoglobin trait follow-up.

The Sickie Cell Training Program courses and workshops are designed to provide up-to-date information about hemoglobin traits, sickle cell disease, and related hemoglobinopathies. The goal of the California statewide program is to promote accurate and appropriate information, education, counseling, testing, and treatment services for infants with hemoglobinopathies. Thank you to our friends in California.

COLORADO

Another state has been extremely helpful to Utah's Newborn Screening Program. I would like to acknowledge the help of Dr. Peter Lane, a hematologist from the University of Colorado, School of Medicine. Donna Holstein, BSN, the hemoglobinopathy educator and counselor that works with Dr. Lane, have consulted with Utah to create the protocols for follow-up of abnormal hemoglobin results. Larry Sater of Colorado's Department of Public Health's Newborn Screening Laboratory provided abnormal hemoglobinopathy specimens to Utah's laboratory to aid in the validation of their IEF test method. Thank you to our friends in Colorado.

Other states that have offered their time and assistance to help Utah develop the hemoglobin follow-up protocols: Arizona, Connecticut, North Carolina, and Ohio.



This is a photo of an isoelectric focusing gel.
The gel contains six control lanes and samples from 40 babies.

Newborn Screening for Sickle Cell Disease and Other Hemoglobinopathies

This entire article is extrapolated from a Consensus Conference held for Newborn Screening for hemoglobinopathies. Conference participants examined questions on the issue of neonatal screening for hemoglobinopathies. Emphasis was placed on enhancing the understanding about hemoglobin screening for all pediatric health care providers, the public, and the National Institutes of Health (NIH). The consensus panel had representatives from the fields of biochemistry, genetics, pediatrics, obstetrics, hematology, public health nursing (This is the field I work in!), law, and epidemiology. The following questions were discussed:

One. Are programs for screening the newborn for sickle cell disease effective in decreasing morbidity and mortality?

Two. What are the techniques of screening and what are their efficacies?

Three. What are the major factors, including the benefits and risks, in hemoglobin newborn screening?

Four. What are the optimal methods of follow-up and management of infants identified with hemoglobinopathies [for disease and carriers (traits)]?

Five. What future research directions are indicated?

The panel arrived at these answers for the questions that were discussed.

One. Although the technology to screen infants in the newborn period has been available for the past 15 years, screening has not received widespread acceptance. It is now known that early diagnosis is the key to preventing morbidity and mortality. There is indisputable evidence of a reduction of complications, especially if the screening process is linked to comprehensive clinical management systems that include parental education. A recent multicenter randomized trial of oral prophylaxis penicillin in infants with sickle cell disease showed an impressive 85% reduction in the incidence of infection in the group treated with oral penicillin compared to the group given a placebo pill. The 13-pneumococcal septic episodes among the 110 in the study group given the placebo pill resulted in three deaths. There were no deaths and only two pneumococcal septic episodes from the 105 infants in the penicillin group. The compelling differences caused the study to be terminated eight months early and prophylactic penicillin was offered to the placebo group.

Because babies with sickle cell disease may develop sepsis as young as four months of age, newborn screening facilitates early detection that leads to comprehensive care. An additional benefit of detection and early intervention is the widespread availability of pneumococcal vaccine. These effective interventions fully justify the newborn screening programs to ensure early access to medical care.

Two. The panel recommends centralized laboratories for universal screening programs and for confirmation of all probable, abnormal hemoglobin screening results. In Utah we will screen with isoelectric focusing and confirm with High Performance Liquid Chromatography (HPLC). The HPLC methodology provides a better resolution of Hemoglobins F, A, S, C, and many other abnormal Hemoglobins. Blood collected from a heel stick and dried on filter paper provides an adequate specimen for screening. Our Utah State Laboratory participates in a quality-control program to ensure proficient screening and testing for hemoglobinopathies.

Three. Good medical practice dictates that newborn screening be available and provided, for all infants, as part of ordinary health care. Instruction on newborn hemoglobinopathy screening should be presented to the parents along with the usual education about the other screening tests

(Congenital Hypothyroidism, Galactosemia, and Phenylketonuria). Public education is critical to an effective screening program. The educator's teachings should help develop a clear understanding of the purpose of hemoglobin screening and include education about the usual screening tests. Educators should outline the nature of sickle cell disease and sickle cell trait.

Each screening program should develop a hemoglobinopathy follow-up protocol. (A copy of Utah's follow-up protocol is published in this newsletter).

Benefits include early detection of disease to facilitate early treatment. There is future health benefit for families to know they have genetic hemoglobin traits.

One risk of hemoglobin screening is the potential anxiety to the family from the discovery that they carry a gene for a hemoglobin trait. This risk can be minimized by careful protocol design and monitoring. Sensitive and sympathetic genetic counseling and education can help the family to deal with their anxiety. Considerable care should be taken to ensure confidentiality of screening results and to maintain the privacy of the family.

The benefits of sickle cell screening, in terms of reduced morbidity and mortality of infants, clearly outweigh the risks of screening.

Four. Comprehensive specialized care should be the right of every infant who is confirmed to have a clinically significant hemoglobinopathy. Economic, social, and cultural factors should be taken into account and be part of the structure for the follow-up program. Pediatric Care Providers should educate themselves about sickle cell disease and about the availability of consultation and support services in their area.

Sickle Cell Diseases. In the first few month's of the child's life, the screening program should help the family establish a network. Components of the ideal network should include Hematologists, Geneticists, genetic counselors, nurse educators, social services, and interpreters. The Pediatric Care Provider should be prepared to:

- ❖ Work with the Department of Health to educate the family and perform the appropriate tests that may be needed to diagnosis sickle cell disease.
- ❖ Initiate the needed steps to insure compliance with the penicillin prophylactic treatment.
- ❖ Administer routine immunizations as well a *Hemophilus influenzae* B vaccine at 18 months of age (with a booster at 2 years of age) and *Streptococcus pneumoniae* by 2 years of age.
- ❖ Monitor growth and development.
- ❖ Monitor optimal nutrition.
- ❖ Help educate families about early identification of symptoms that could lead to serious complications (fever, lethargy, pallor, and enlarging abdomen).
- ❖ Make the proper referrals for insurance purposes.
- ❖ Facilitate access to a tertiary care center for emergency inpatient services.

Other Hemoglobinopathies that require specialized clinical care are outlined in the "Utah's Hemoglobinopathy Reporting Table," published in this newsletter. Carrier (Trait) identification will have education provided that explains that the carrier (trait) state is not a disease.

Five. Further research should focus on the following: defining the impact of the social, cognitive, and emotional development of the child and family members; assessing methods of management for infection; and providing optimal education of individuals and families at risk.

In summary, the panel concludes that every child should be screened for hemoglobinopathies to prevent the potentially fatal complications of sickle cell disease during infancy.

UTAH DEPARTMENT OF HEALTH GUIDELINES FOR FOLLOW-UP OF HEMOGLOBINOPATHIES

The primary purpose of Hemoglobinopathy screening is the identification of infants with sickle cell diseases for whom early intervention has been shown to markedly reduce morbidity and mortality. Hemoglobinopathies are complex disorders and pediatric care physicians (PCP) are strongly encouraged to refer their patients to pediatric hematologists for treatment. Detection of infants with hemoglobin traits (genetic carriers of hemoglobin disease) creates an opportunity for genetic counseling and the identification of couples, at risk, for having children born with hemoglobin disease.

FOLLOW-UP OF INFANTS WITH PROBABLE HEMOGLOBIN DISEASE Newborn Screening Results FS, FSC, FSA, F only, FU, etc.**

1. The Utah State Laboratory will screen for hemoglobinopathies on the first blood spot specimen submitted on each infant.
 - a. The laboratory will screen the first specimen for hemoglobinopathies using isoelectric focusing (IEF).
 - b. Any screen that shows hemoglobin bands that are suggestive of abnormal hemoglobin or that have atypical banding patterns, will be retested, with IEF, using the same dried blood spot specimen.
 - c. The lab will report probable, positive/abnormal hemoglobin results, within 72 hours, to the Newborn Screening Program's (NSP) follow-up (FU) coordinator.
 - d. The first screen mailers will include hemoglobin-screening results.
 - e. The Lab will use the second newborn screening blood spot specimen submitted to confirm abnormal first screening results. Confirmation will be done using High Performance Liquid Chromatography (HPLC) instruments and will be interpreted by a pediatric hematologist.
2. Within ten (10) days, the follow-up coordinator:
 - a. Notifies the Department of Hematology of the potential abnormal hemoglobin screening result and that the confirmation process has started. A copy of the follow-up letters will be forwarded to Shirley Bleak, FNP-C in Hematology.
 - b. Notifies the PCP by telephone and in writing (by a faxed and/or mailed template letter). All of the steps taken to notify the PCP of the abnormal results will be documented. It will be the PCP's responsibility (or choice) to notify the family about the presumptive test results. The PCP, family, and NSP coordinator will work in concert to facilitate the confirmatory testing.
 - c. Letters to the PCP and family will explain the confirmation process and provide some basic education about the presumptive test results. A copy of "Utah's Hemoglobinopathy Reporting Table" will be included with the letter.
 - d. The follow-up file will be closed after receiving a diagnostic summary form from PCP, genetic counselor, or Hematologist.

e. After confirmation hemoglobin results are received, education and written information about the hemoglobin disorder, genetics, and treatment will be provided to the PCP and the family. Education should be sensitive to cultural and social needs of the family.

FOLLOW-UP OF INFANTS WITH PROBABLE HEMOGLOBIN TRAITS

Newborn Screening Results FAS, FAC, FAU (slow), FAU (fast), etc.**

Same procedures as steps 1 and 2 listed above. Education about the hemoglobin trait (variant) and the genetics will be provided to the PCP and families.

The family's referral to genetics for hemoglobin trait counseling will be coordinated between the PCP, genetics department, and the follow-up coordinator.

FOLLOW-UP GUIDELINES FOR TRANSFUSIONS AND HEMOGLOBINOPATHIES (AF)**

A newborn screening blood spot sample should always be obtained prior to giving a blood transfusion. Isoelectric Focusing may show more hemoglobin A than Hemoglobin F. Samples that show more A than F hemoglobin suggest that the infant might have had a blood transfusion. For about one-third of hemoglobin AF screening results, the infant did NOT have a blood transfusion. Blood transfusions may lead to abnormal results. In the cases where the blood spot sample is collected AFTER a blood transfusion:

1. The follow-up coordinator will call and document, from the infants medical records, the dates of transfusions and the newborn screening specimen collection date.
2. If the blood transfusion was given BEFORE collecting the first screening specimen, the transfusion follow-up coordinator will arrange to repeat the first screening specimen, with help of the PCP, in four months (120 days). This follows the same time line for repeating post transfusion Galactosemia testing (GALT).
3. A file will be created to track the post transfusion time.
4. The transfusion follow-up file will be closed after receiving the 120-day, repeat recall-screening specimen.
5. If the medical record shows that the infant has NOT had a transfusion there will be NO transfusion follow-up.

CONFIDENTIALITY

All information, forms, files, and laboratory reports will be treated as confidential.

**Hemoglobins (Hb) are reported in order of quantity FSA=F>S>A

Hb A=Adult hemoglobin

Hb F=Fetal hemoglobin

Hb S=Sickle hemoglobin

Hb C=Hemoglobin C

U=Unidentified hemoglobin

UTAH'S HEMOGLOBINOPATHY REPORTING TABLE

Common Hemoglobin Lab Results*	Explanation Hemoglobin Pattern	Likely Causes (Possible Conditions)	Clinical Manifestations	Specialized Clinical Care Required	Referral Recommended
FA	No abnormal hemoglobin detected	Normal	None	None	None
FS (noA)	Sickle cell disease SS or Sickle • - thalassemia	Hb SS Hb S •°- thal Hb S • + thal	Severe Severe Mild to Moderate	Yes with ** Yes with ** Yes with **	Hematology Hematology Hematology
FSC (noA)	Infant probably having sickle C disease (hemoglobin SC disease)	Sickle-hemoglobin C disease	Moderate to Severe	Yes **	Hematology
FSA	Sickle • - thalassemia or sickle cell anemia AFTER BLOOD TRANSFUSION	Hb S β+ thal Hb SS after transfusion	Mild to Moderate	Yes **	Hematology
FC (no A)	Hemoglobin CC or Hemoglobin C • - thal	Homozygous hemoglobin C	Mild hemolytic anemia	Varies **	Hematology
FAS	Sickle cell trait (carrier)	Infant inherited one sickle cell gene	Asymptomatic	None **	Education & Genetic Counseling
FAC	Hemoglobin C trait (carrier)	Infant inherited one hemoglobin C gene	Asymptomatic	None **	Education & Genetic Counseling
FAU (slow)	Unidentified slow migrating band	Hb E, Hb O, Hb D, or Hb G TRAIT	None to mild anemia	Confirmatory testing needed	Education & Genetic Counseling
FAU (fast)	Unidentified fast migrating band	Hb Bart's (• - thalassemia)	None to mild anemia	Confirmatory testing needed	Education & Genetic Counseling
F only	Premature infant or possible • - thalassemia			Repeat Screening	Education & Genetic Counseling
AF (More A than F)	Transfused infant or normal infant	Specimen collected <i>after</i> transfusion		If transfused- repeat screen in 120 days	

Abbreviations: F = fetal hemoglobin S = sickle hemoglobin • = Beta • = Alpha
A = adult hemoglobin C = hemoglobin C "thal" = thalassemia

* Hemoglobins (Hb) are reported in order of quantity (example: FSA = F>S>A)

** Confirmatory Testing Needed (Arranged through the Department of Health, call 801-584-8260)

Questions: Call Department of Health, Newborn Screening 801-584-8260, Department of Hematology 801-588-2680, or Division of Medical Genetics 801-581-8943

Fill in the sample collection date on the newborn screening forms

The Newborn screening program has recently received a plethora of forms *without* the sample collection date. The follow-up program must call to collect the dates, at the rate of, at least 50 (and sometimes more), blood spot specimens each day. (Eight percent-this is way-too-many!) The sample collection date is needed by the lab to determine if the specimen falls within the two week time period. This is a Clinical Laboratory Improvement Act of 1988 (CLIA) regulation. If we *can't* discover the specimen collection date, the specimen will be rejected, marked UNSATISFACTORY and you start over. **PLEASE-FILL OUT THE FORM-COMpletely!**

Utah Department of Health
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RETURN SERVICES REQUESTED

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